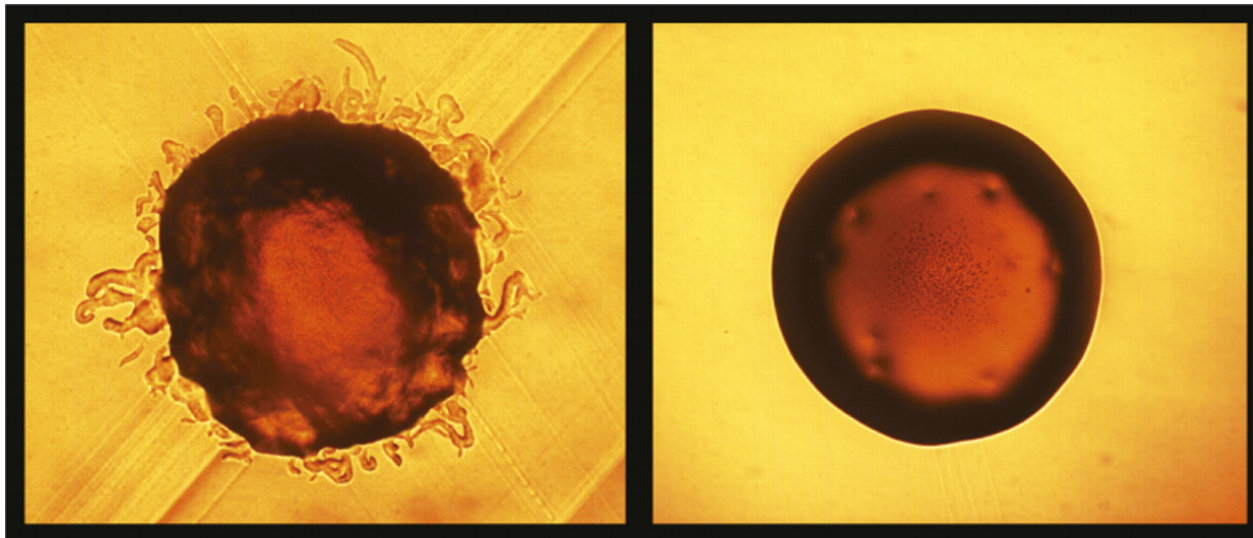


Evolutionary dynamics of *Pseudomonas aeruginosa* in persistent Cystic fibrosis airway infections

Lars Jelsbak

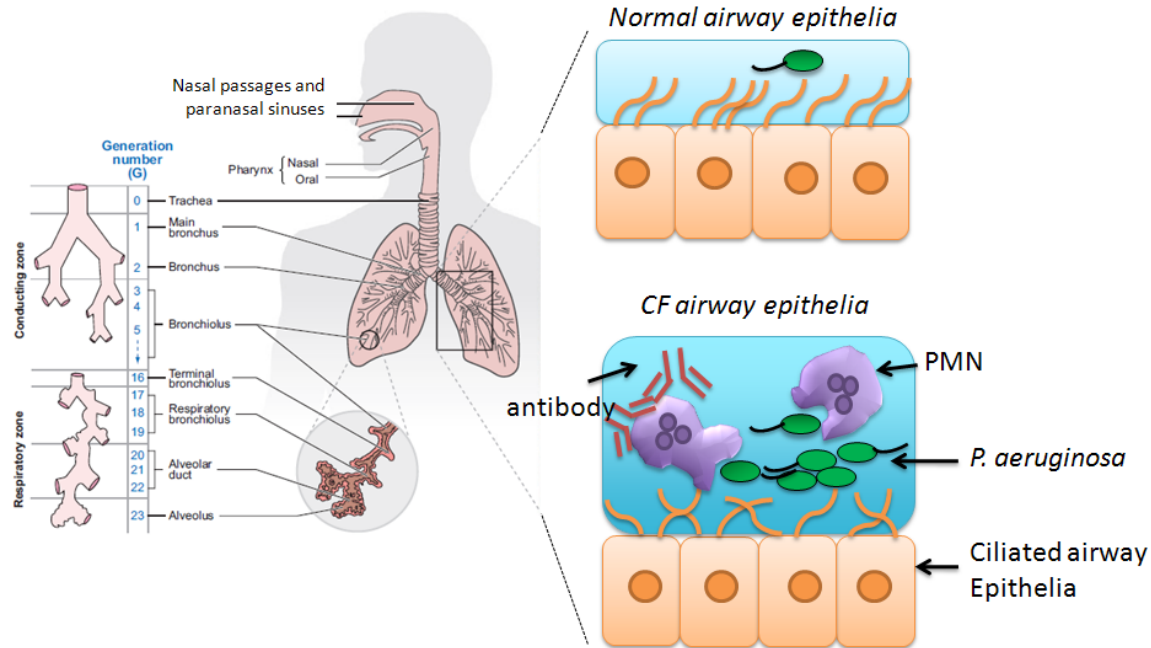
Technical University of Denmark



P. aeruginosa isolate sampled in 1973 (*Left*) and a clonal descendant isolated 35 years (~200,000 generations) later (*Right*)

Pseudomonas aeruginosa infections in Cystic fibrosis patients

- CF is caused by mutations in the *CFTR* gene which affect chloride channels.
- This results in decreased fluidity of mucus
-> Impaired clearance microbes



CF patients typically develop persistent *Pseudomonas aeruginosa* lung infections that lead to reduced lung function.

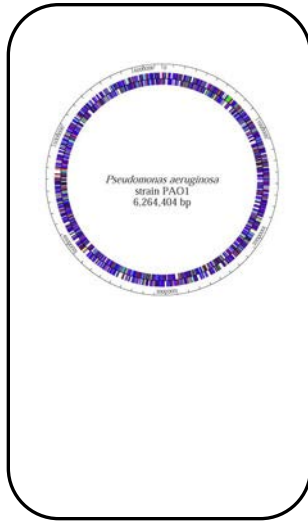
CF airways are highly differentiated ecosystems:

- Spatial heterogeneity
- Chemical complexity
- Non-uniform distributions of resources

Evolution by natural selection is an inevitable and inescapable feature of life.

Physiological adaptation

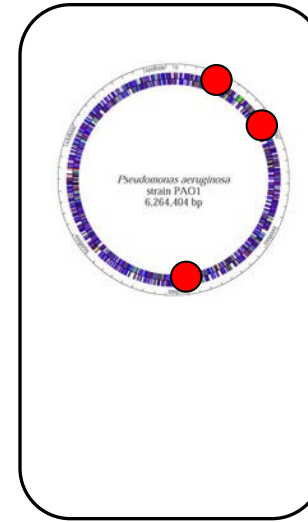
Virulence genes
Gene expression
Regulatory networks



The genetic inventory (the genome) of a particular micro-organism outlines the boundaries of performance in relation to a specific infection type.

Genetic adaptation

Mutation and
Natural selection



The possibility of adaptive and evolutionary events constitutes the interactive development of the microbial population within its host environments.

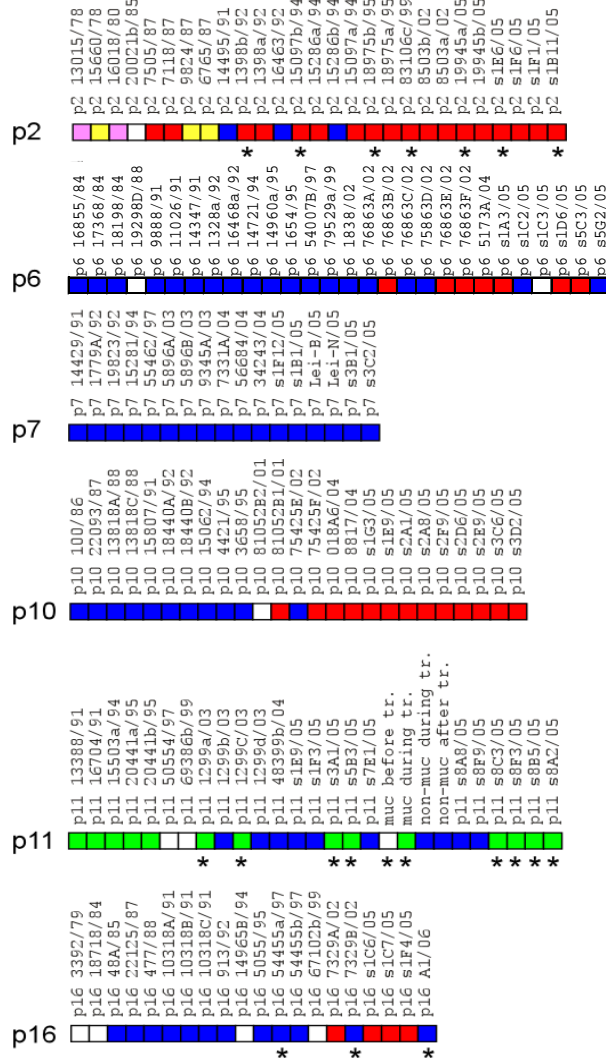
Microbes that cause (chronic) infections undergo genetic change as they adapt to selective pressures encountered in host tissues.

CF evolutionary model system

- Dynamics and mechanisms by which *P. aeruginosa* adapt to the CF host ?

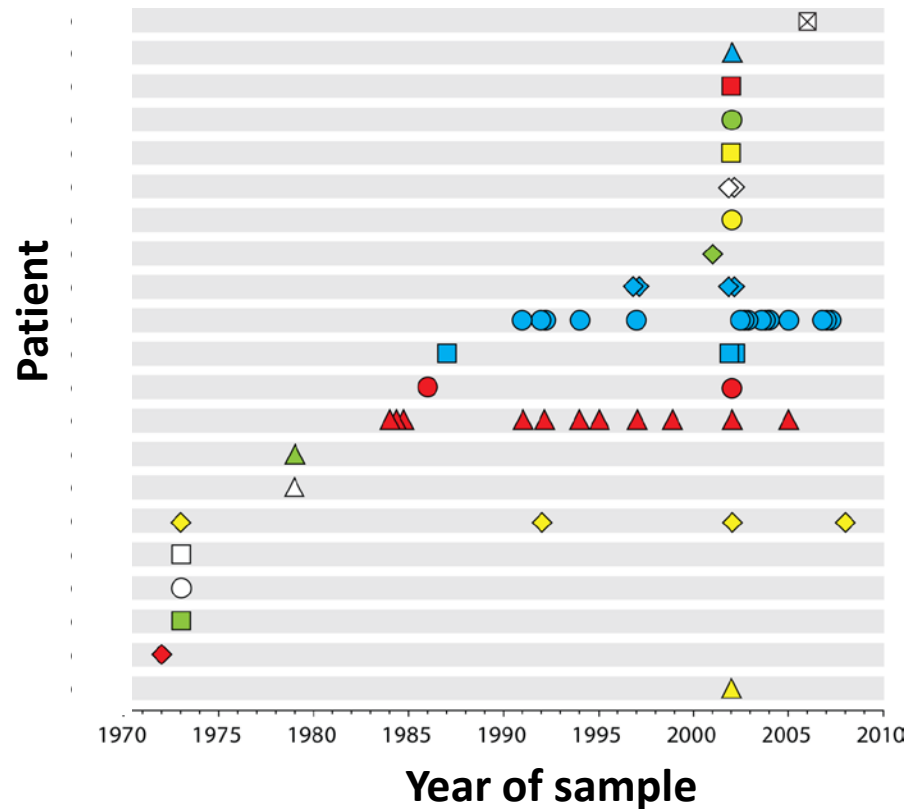
DK1

Two transmissible and competitive *P. aeruginosa* lineages : DK1 and DK2



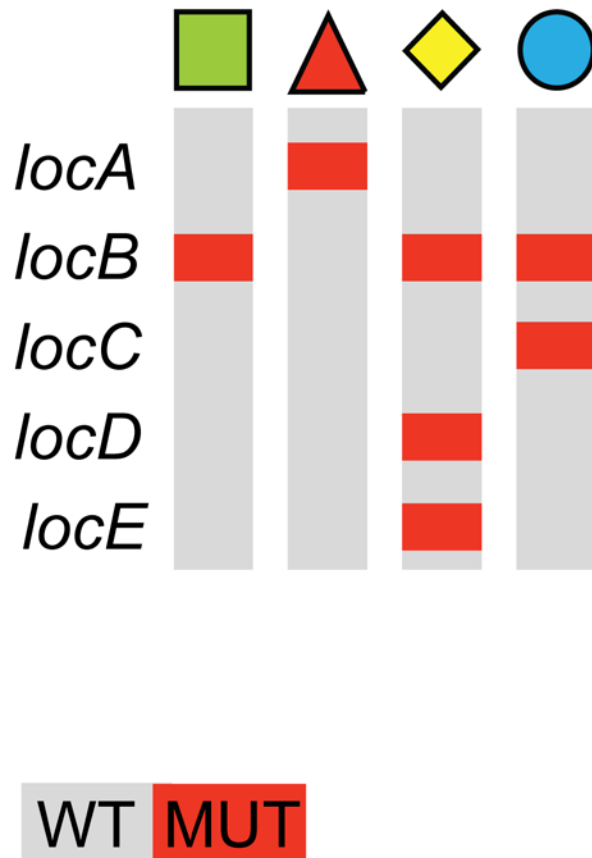
- Niels Høiby founded in 1973 a unique collection of *Pseudomonas aeruginosa* bacteria isolated from CF patients at the Copenhagen CF Clinic. This collection is still expanding and is a gold mine of 'fossils' for studies of microbial evolution
- Identification of two lineages found in many different patients since 1973
- Transmissible and competitive
- DK1 and DK2 have successfully persisted for 4 decades in many different CF patients.

The genomes of 55 isolates of the DK2 clone type were sequenced to track 40 years of genomic evolution

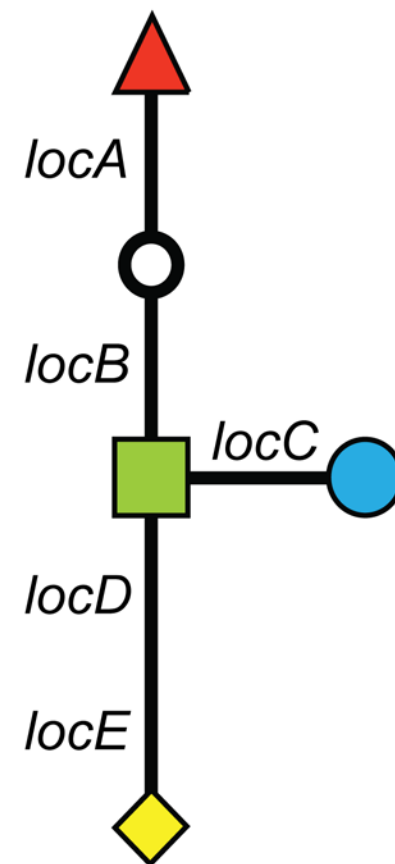


Genome sequencing of DK2 isolates – identification of SNPs and construction of phylogenetic tree:

Genotype of clones

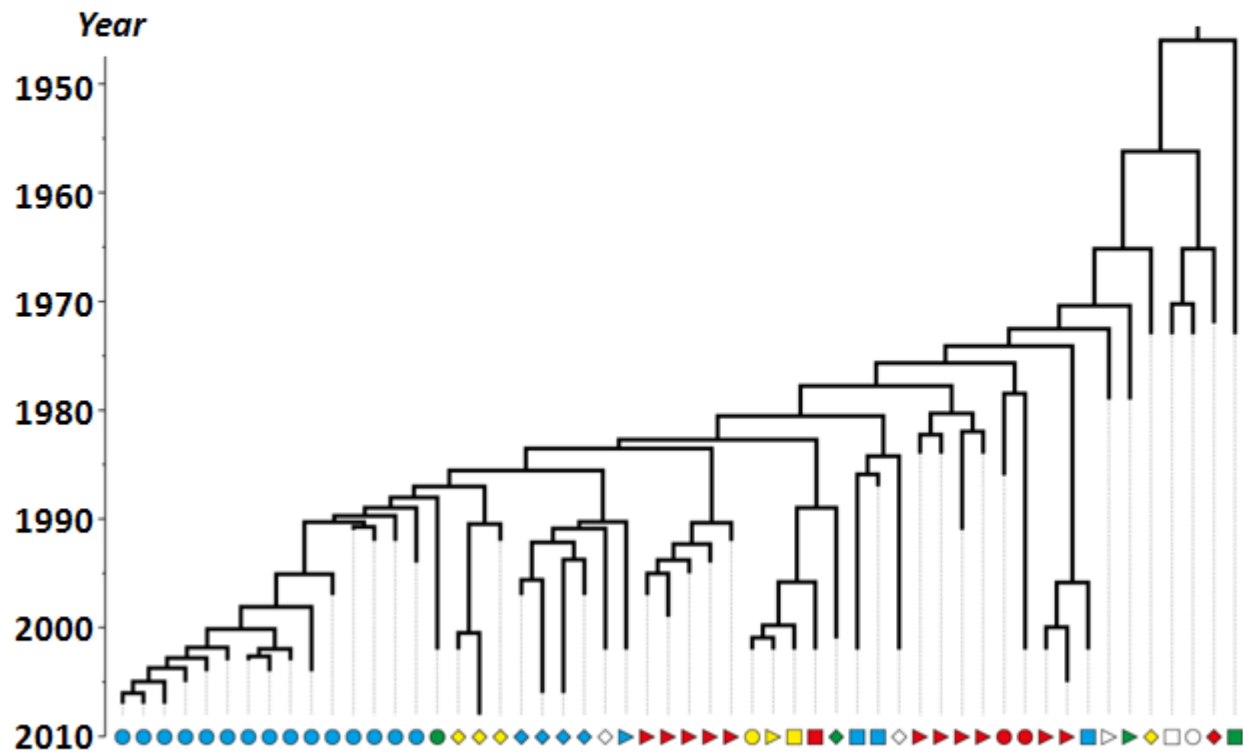


Genetic relationship



SNP based phylogenetic tree representing the evolutionary relationship among DK2 isolates

Bayesian analysis
(BEAST) used to
estimate divergence
times



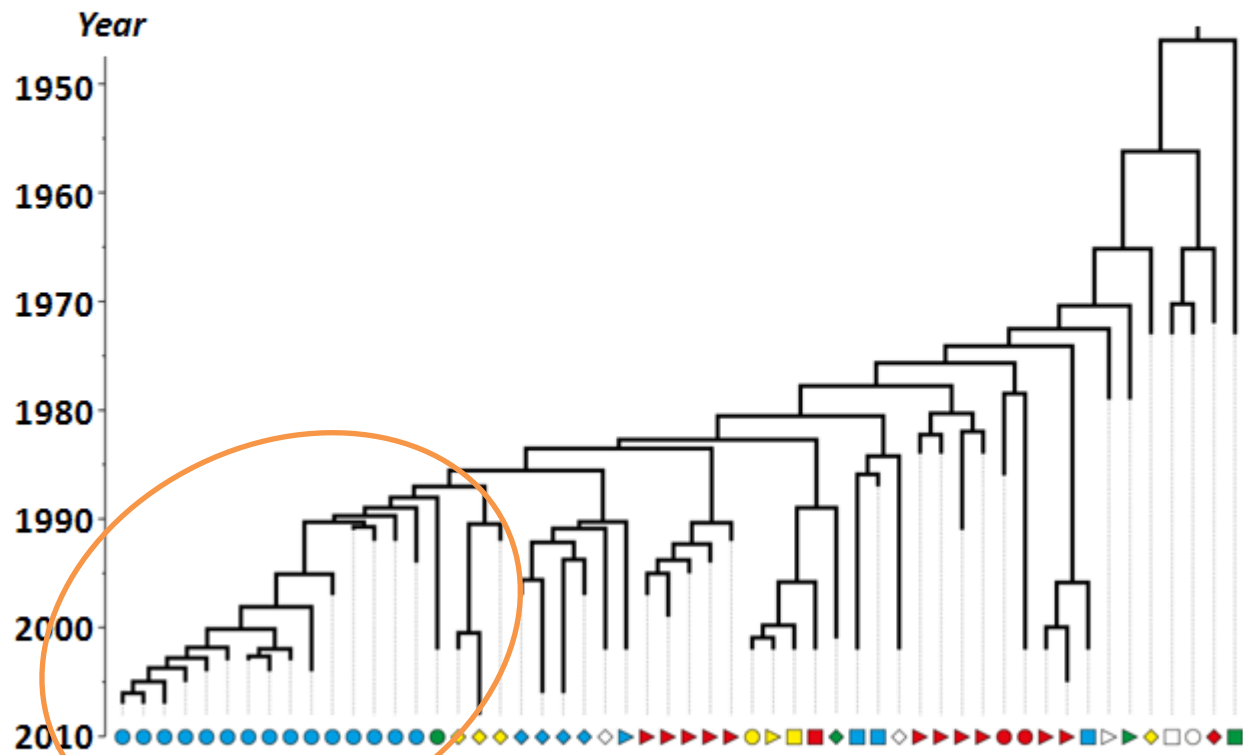
Highly consistent, few homoplastic sites



Rasmus Marvig
(CT34)

SNP based phylogenetic tree representing the evolutionary relationship among DK2 isolates

Bayesian analysis
(BEAST) used to
estimate divergence
times



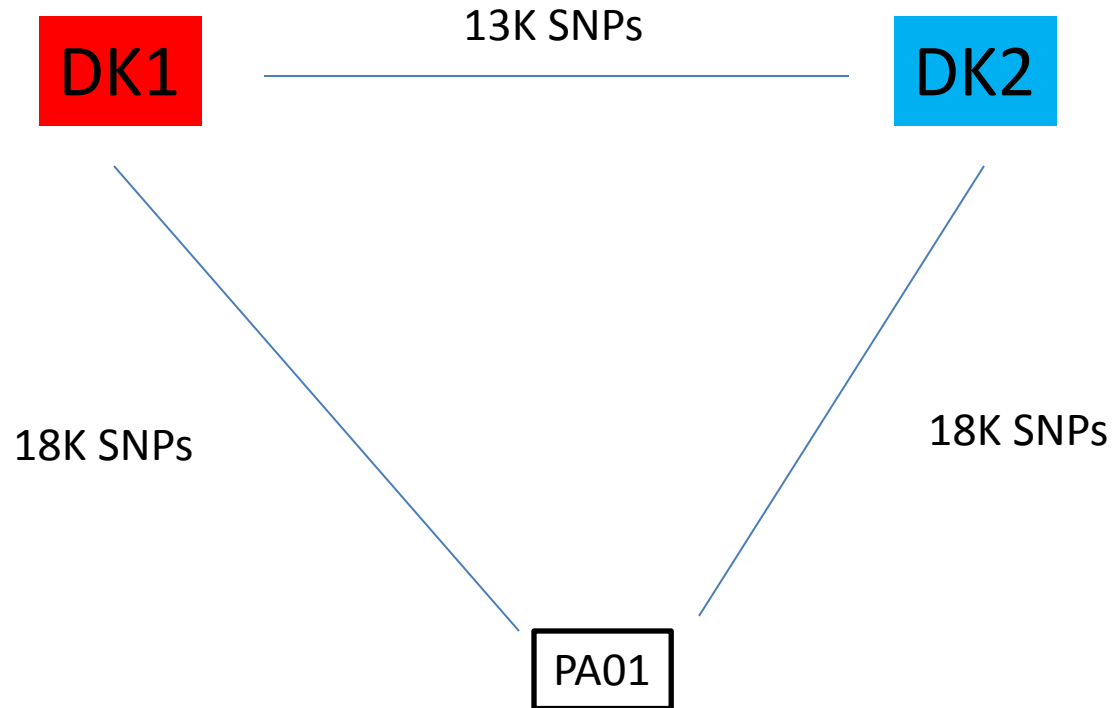
Limited diversification despite structured environment



Rasmus Marvig
(CT34)

DK1 and DK2 are distinct lineages

Genome comparisons:



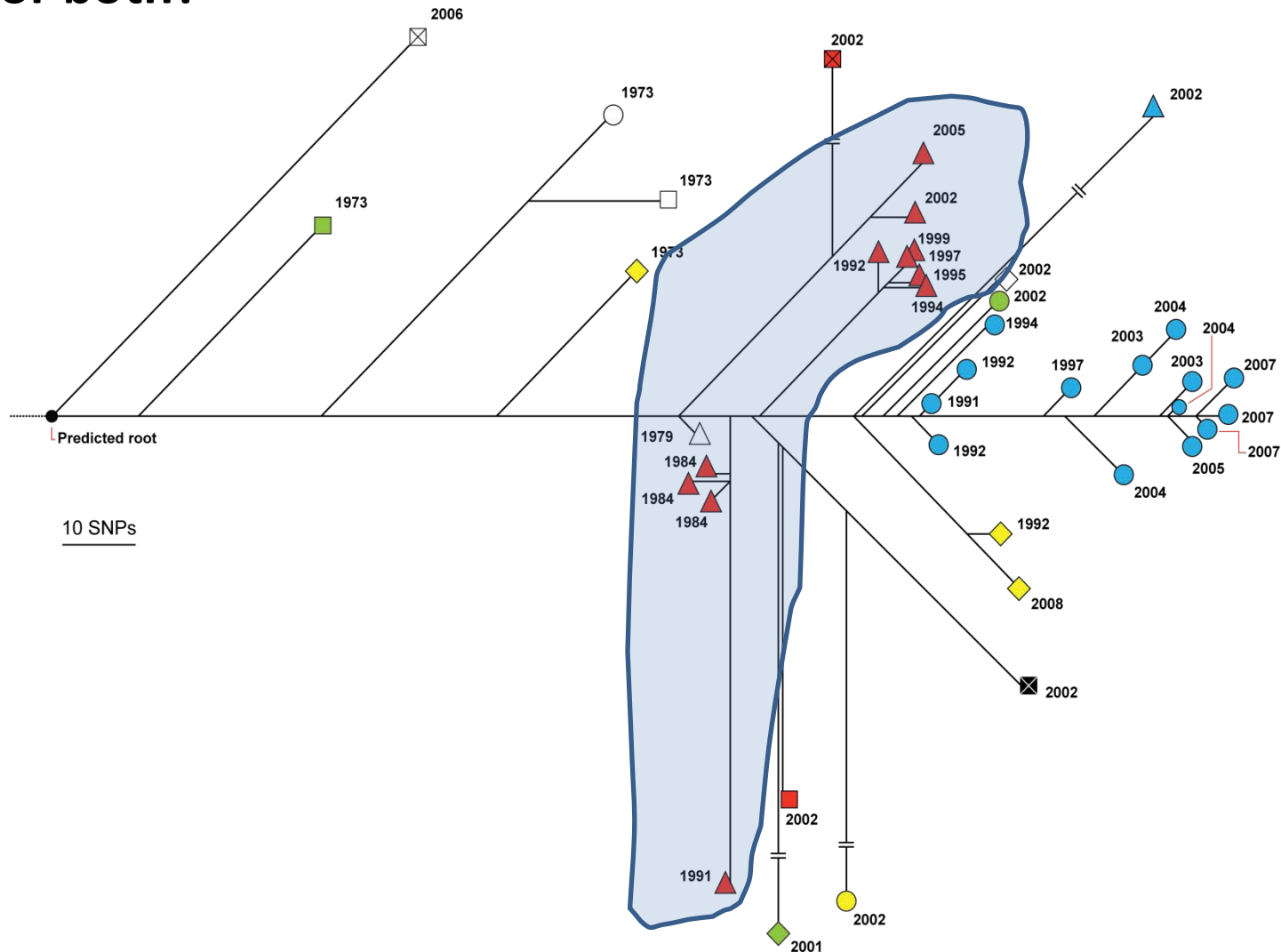
Two examples of interaction between DK1 and DK2

Competition in the CF lung?

Horizontal transfer of DNA

Population dynamics

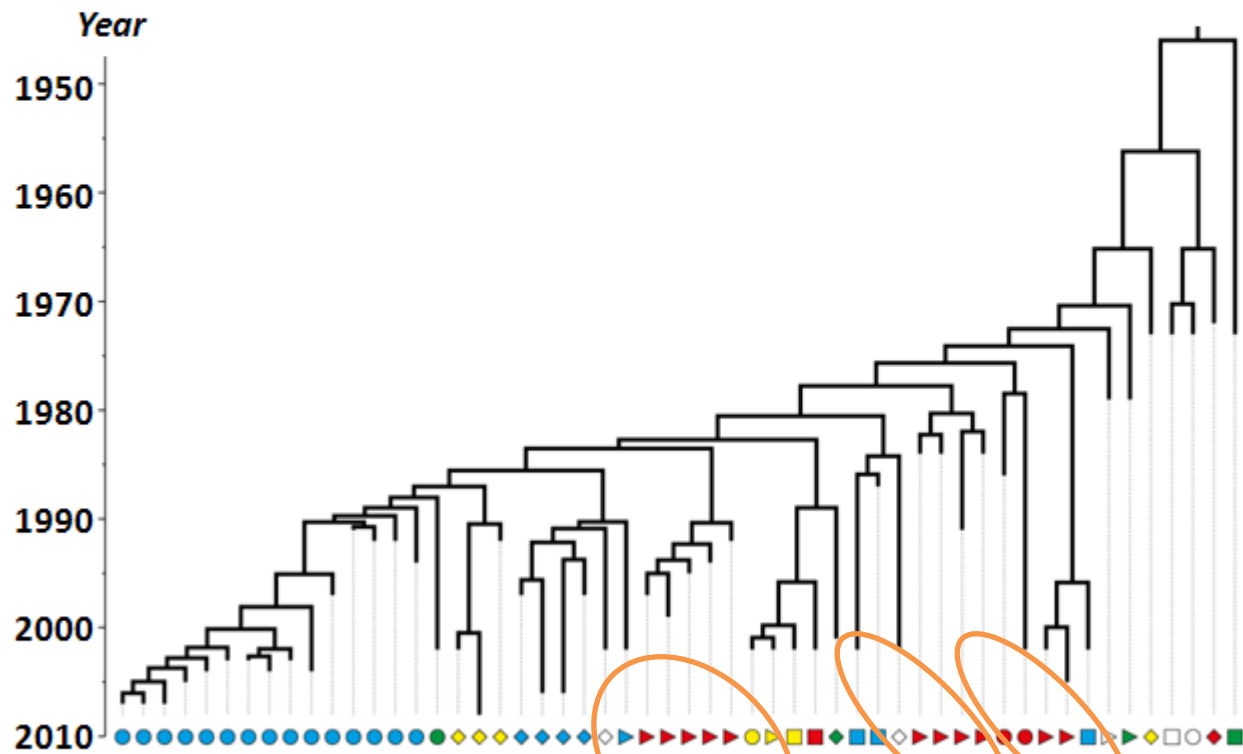
Different transmission events or variants rising in frequency or both?



Population dynamics

Different transmission events or variants rising in frequency or both?

Bayesian analysis (BEAST) used to estimate divergence times



Limited diversification despite structured environment

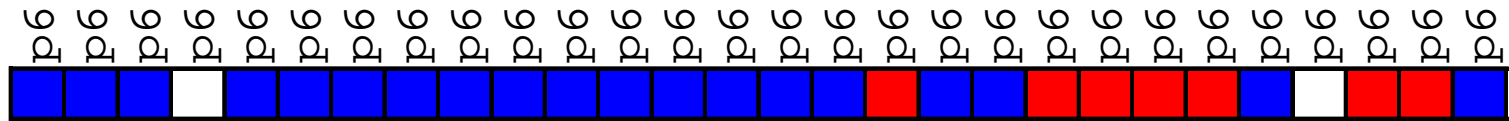


Rasmus Marvig
(CT34)

DK2

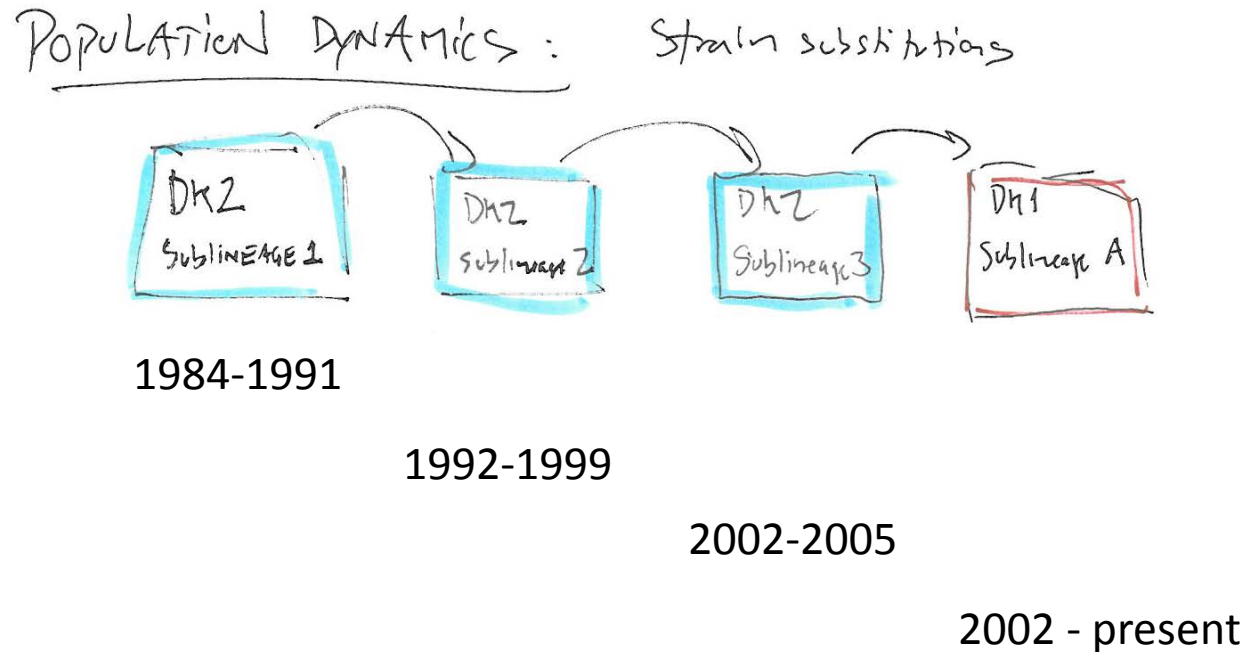
DK1

This patient has been co-infected by both the DK-1 (red) and the DK-2 (blue) lineages



2011: Only DK1 – no sign of any DK2 present

Inter- and intracolon competition in the CF lung?



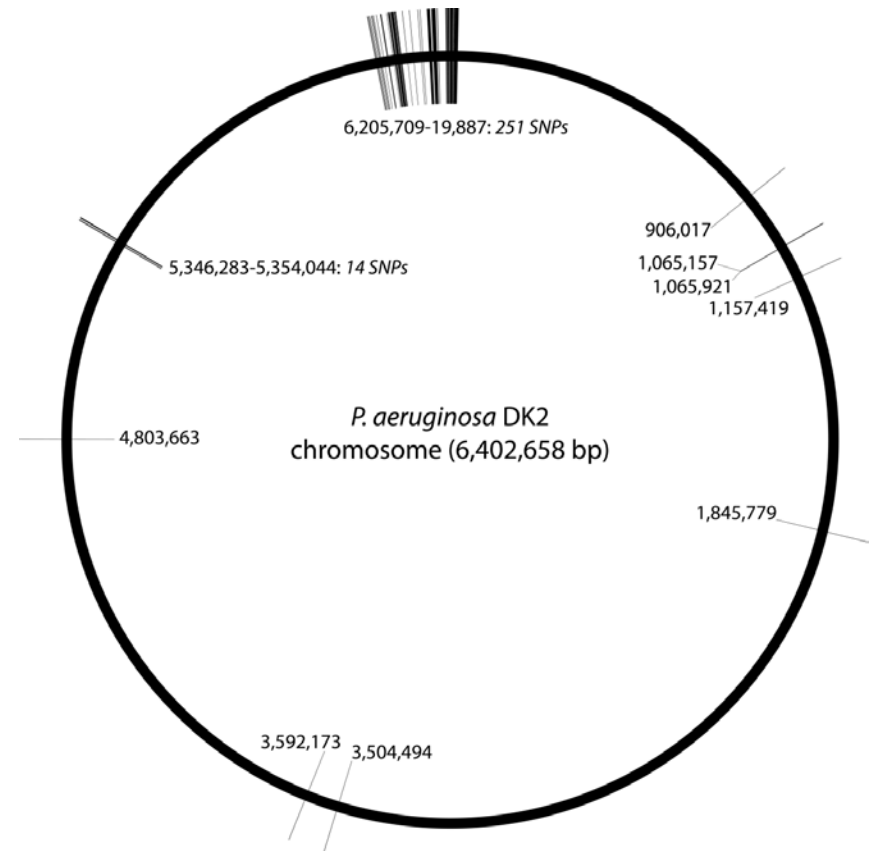
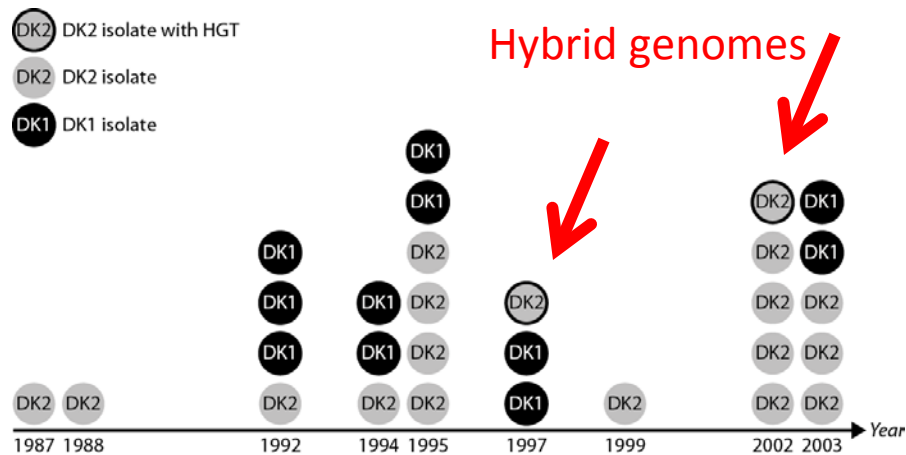
Eradication of lineages that cannot be cleared from the patients by medical intervention

Two examples of interaction between DK1 and DK2

Competition in the CF lung?

Horizontal transfer of DNA

Horizontal gene transfer events can be inferred from non-random distribution of SNPs



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